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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,875	08/01/2003	Raymond F. Schinazi	60137.0017USU1	3042

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EXAMINER	
OLSON, ERIC	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/632,875	SCHINAZI ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-40 and 42-75* is/are pending in the application.

4a) Of the above claim(s) *61-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-40 and 42-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted April 6, 2007 wherein claims 31, 39, 40, 42-46, 52, 54, 56, 58, and 59 are amended, claims 1-30, 41, and 53 are cancelled, and new claims 61-75 are introduced. This application claims benefit of provisional applications 60/453715, filed August 1, 2002, and 60/453716, filed August 1, 2002.

Claims 31-40, 42-52, and 53-75 are pending in this application.

New claims 61-75 are withdrawn from consideration as belonging to a non-elected invention.

Claims 31-40, 42-52, and 53-60 as amended are examined on the merits herein.

Applicant's amendment, submitted April 6, 2007, with respect to the objection to instant claims 40 and 42 for containing improper punctuation, has been fully considered and found to be persuasive to remove the objection as the claims have been amended to correct the error. Therefore the objection is withdrawn.

Applicant's application data sheet, submitted April 6, 2007, is persuasive to remove the objection to the disclosure for lacking reference to provisional application 60/453716 in the first paragraph of the specification. Specifically, the application no longer claims priority to 60/45316. Therefore the objection is withdrawn.

Applicant's amendment submitted April 6, 2007, with respect to the rejection of instant claims 31-45 and 58-60 under 35 USC 112, first paragraph, for lacking enablement for a method of prophylaxis, has been fully considered and found to be persuasive to remove the rejection as the claims as amended no longer recite a method of prophylaxis. Therefore the rejection is withdrawn.

Applicant's amendment submitted April 6, 2007, with respect to the rejection of instant claims 31-38, 40, 42-45, 46-50, 52, and 54-60 under 35 USC 112, second paragraph, for reciting the indefinite phrases, "such as" and "capable of", has been fully considered and found to be persuasive to remove the rejection as the claims as amended no longer recite said indefinite phrases. Therefore the rejection is withdrawn.

Applicant's amendment submitted April 6, 2007, with respect to the rejection of instant claims 31-60 under 35 USC 102(e) for being anticipated by Mueller et al., has been fully considered and found to be persuasive to remove the rejection as the claims as amended no longer disclose the chemical species recited by Mueller et al. Therefore the rejection is withdrawn.

Applicant's amendment submitted April 6, 2007, with respect to the rejection of instant claims 31-35, 39-42, 46-56, and 58-60 under 35 USC 102(b) for being anticipated by Lin et al., (US patent 5627160) has been fully considered and found to be

persuasive to remove the rejection as the claims as amended no longer disclose the chemical species recited by Lin et al. Therefore the rejection is withdrawn.

Applicant's amendment submitted April 6, 2007, with respect to the rejection of instant claims 31-35, 39-42, 46-56, and 58-60 under 35 USC 102(e) for being anticipated by Lin et al., (Biochemical Pharmacology, Vol. 47, no. 2, pp. 171-174, 1994) has been fully considered and found to be persuasive to remove the rejection as the claims as amended no longer disclose the chemical species recited by Lin et al. Therefore the rejection is withdrawn.

Applicant's amendment submitted April 6, 2007, with respect to the rejection of instant claims 31-60 under 35 USC 102(b) for being anticipated by Schnazi et al., has been fully considered and found to be persuasive to remove the rejection as the claims as amended no longer disclose the chemical species recited by Schnazi et al. Therefore the rejection is withdrawn.

Applicant's amendment submitted April 6, 2007, with respect to the rejection of instant claims 31-35, 39-42, and 46-54 under 35 USC 102(b) for being anticipated by Gagnon et al., has been fully considered and found to be persuasive to remove the rejection as the claims as amended no longer disclose the chemical species recited by Gagnon et al. Therefore the rejection is withdrawn.

Applicant's amendment submitted April 6, 2007, with respect to the rejection of instant claims 31-35, 39-42, and 46-54 under 35 USC 102(b) for being anticipated by Locatelli et al., has been fully considered and found to be persuasive to remove the rejection as the claims as amended no longer disclose the chemical species recited by Locatelli et al. Therefore the rejection is withdrawn.

The following new grounds of rejection are introduced:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 31-38, 46-50, 52, and 55-60 are rejected under 35 U.S.C. 102(e) as being anticipated by Stuyver et al. (PCT international publication WO02/32920, reference included with PTO-1449) Stuyver et al. discloses a class of nucleoside compounds that encompasses the nucleosides of the claimed invention. (p. 16, compound I-a, p. 18, compound III-a) A specific embodiment is disclosed in which the nucleoside is a β-L-2',3'-dideoxycytosine nucleoside. (p. 48, paragraphs 1 and 2, D = H, acyl, monophosphate, or monophosphate ester) Pharmaceutical compositions containing

these compounds are suitable for treating viral infections such as *Flaviviridae*, (p. 73, last paragraph) particularly HCV. (p. 78, first paragraph) The nucleosides can be administered in combinations with other antiviral agents, (p. 77, second paragraph) including interferon and ribavirin as well as other anti-HCV agents. (pp. 78-80) Additionally, it is noted that the intended use of the claimed compositions is not critical to patentability, as any composition having the same components in the same amounts is reasonably expected to be useful for the same purpose.

Therefore the invention is anticipated by Stuyver et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 39, 40, 42-45, 51, and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stuyver et al. (PCT international publication WO02/32920, reference included with PTO-1449) The disclosure of Stuyver et al. is discussed above. Also note that, in the generic formula disclosed by Stuyver et al., the embodiments of formula I-a in which R1 = lower alkenyl, lower alkynyl, aryl, CN, or NO_2, R1' – R2 = R2' = R3 = R3' = H, Y1 = O, X1 = NHR^4, R4 = lower alkyl or lower alkenyl, and D – H, alkyl, monophosphate, or acyl fall within the claimed invention and bear a close structural resemblance to the dideoxy cytosine compound pictured on p. 48. Furthermore, the

other identities of D recited by Stuyver et al. are reasonably considered to be pharmaceutically acceptable leaving groups according to the instant claims. Stuyver et al. does not specifically embody a composition containing a nucleoside having the specific 4-N- or 5- modifications recited by the instant claims.

It would have been obvious to one of ordinary skill in the art at the time of the invention to make the pharmaceutical compositions comprising the nucleosides of claims 39, 40, 42-45, 51, and 54. One of ordinary skill in the art would have been motivated to practice the invention in this manner because these nucleosides are already included within the broad teaching of Stuyver et al. One of ordinary skill in the art would reasonably have expected success because these compounds bear a close structural similarity to species explicitly recited by Stuyver et al.

Therefore the invention taken as a whole is *prima facie* obvious.

Claims 31-38, 46-50, 52, and 55-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gagnon et al. (Reference of record in previous office action) in view of Gosselin et al. (PCT international publication WO00/26225, Reference included with PTO-892) Gagnon et al. discloses the nucleosides β-L-dideoxycytidine and β-L-5-fluoro-dideoxycytidine. (p. 20, figure 1) These compounds were shown to possess antiviral activity. (p. 21, last paragraph) Gagnon et al. does not disclose pharmaceutical compositions comprising the monophosphates or other pharmaceutically acceptable leaving groups of these nucleosides.

Gosselin et al. discloses β-L-2-azido fluorocytidine nucleosides having a structure similar to the dideoxy nucleosides of Gagnon et al. (p. 4, bottom of page) These nucleosides can also be prepared as 5'-O- phosphates. These nucleosides are useful as antiviral agents. (p. 5, lines 10-17)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the nucleosides of Gagnon et al. by adding a 5'-O- phosphate. One of ordinary skill in the art would have been motivated to do so because Gosselin et al. discloses that nucleoside phosphates having a similar structure are useful as antiviral agents. One of ordinary skill in the art would reasonably have expected success because phosphates are a common and routine prodrug moiety to attach to nucleosides.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 31-38, 46-50, 52, and 55-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Locatelli et al. (Reference of record in previous office action) in view of Gosselin et al. (PCT international publication WO00/26225, Reference included with PTO-892) Locatelli et al. discloses the nucleoside β-L-dideoxycytidine. (p. 685, figure 2) This compound is disclosed to be a promising antiviral agent. (p. 684, first paragraph) Locatelli et al. does not disclose pharmaceutical compositions comprising the monophosphates or other pharmaceutically acceptable leaving groups of these nucleosides.

Gosselin et al. discloses β-L-2-azido fluorocytidine nucleosides having a structure similar to the dideoxy nucleosides of Locatelli et al. (p. 4, bottom of page) These nucleosides can also be prepared as 5'-O- phosphates. These nucleosides are useful as antiviral agents. (p. 5, lines 10-17)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the nucleosides of Locatelli et al. by adding a 5'-O- phosphate. One of ordinary skill in the art would have been motivated to do so because Gosselin et al. discloses that nucleoside phosphates having a similar structure are useful as antiviral agents. One of ordinary skill in the art would reasonably have expected success because phosphates are a common and routine prodrug moiety to attach to nucleosides.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 31-38, 40, 42-50, 52, and 54-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schinazi et al. (US patent 5990093, Reference of record in previous office action) Schinazi et al. discloses the nucleoside β-L-5-fluorodideoxycytidine and other 5-halo dideoxycytidine compounds. (column 2, lines 18-52) This compound is disclosed to be an antiviral agent useful in pharmaceutical compositions for treating HBV. (column 3, lines 8-18) Schinazi et al. also discloses prodrugs of the dioxolane of β-L-5-fluorodideoxycytidine in which the 5-O- position is derivatized with alkyl, acyl, amino acids, or phosphate, and the 4-N- position is derivatized with an alkyl or acyl group, and also generally teaches that the disclosed

nucleosides can be administered as prodrug derivatives. (column 5, lines 10-67) Schinazi et al. does not disclose pharmaceutical compositions comprising the monophosphates or other pharmaceutically acceptable prodrugs of β-L-5-fluorodideoxycytidine.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the β-L-5-fluorodideoxycytidine nucleosides of Schinazi et al. by the same 4-N- and 5'-O- modifications applied to the dioxolane nucleoside in column 5, lines 10-67 to form a prodrug. One of ordinary skill in the art would have been motivated to do so because Schinazi et al. discloses that these modifications produce useful prodrugs of the similar dioxolane nucleosides. One of ordinary skill in the art would reasonably have expected success because phosphates and alkyl groups are a common and routine prodrug moiety to attach to nucleosides.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 31-38, 46-50, 52, and 55-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin et al. (Reference of record in previous office action) in view of Gosselin et al. (PCT international publication WO00/26225, Reference included with PTO-892) Lin et al. discloses the nucleosides β-L-dideoxycytidine and β-L-5-fluoro-dideoxycytidine. (p. 172, second paragraph) This compound is disclosed to be a promising antiviral agent. (p. 173, third paragraph) Lin et al. does not disclose pharmaceutical compositions comprising the monophosphates or other pharmaceutically acceptable leaving groups of these nucleosides.

Gosselin et al. discloses β-L-2-azido fluorocytidine nucleosides having a structure similar to the dideoxy nucleosides of Locatelli et al. (p. 4, bottom of page) These nucleosides can also be prepared as 5'-O- phosphates. These nucleosides are useful as antiviral agents. (p. 5, lines 10-17)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the nucleosides of Lin et al. by adding a 5'-O- phosphate. One of ordinary skill in the art would have been motivated to do so because Gosselin et al. discloses that nucleoside phosphates having a similar structure are useful as antiviral agents. One of ordinary skill in the art would reasonably have expected success because phosphates are a common and routine prodrug moiety to attach to nucleosides.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 31-38, 46-50, 52, and 55-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin et al. (US patent 5627160, Reference of record in previous office action) in view of Gosselin et al. (PCT international publication WO00/26225, Reference included with PTO-892) Lin et al. discloses compounds and pharmaceutical compositions that are useful for treating viral infections including HBV. (column 3, line 17 – column 4, line 37) Embodiments of this invention include the nucleosides β-L-dideoxycytidine and β-L-5-fluoro-dideoxycytidine. (column 5, lines 33-52) Lin et al. does not disclose pharmaceutical compositions comprising the monophosphates or other pharmaceutically acceptable leaving groups of these nucleosides.

Gosselin et al. discloses β-L-2-azido fluorocytidine nucleosides having a structure similar to the dideoxy nucleosides of Locatelli et al. (p. 4, bottom of page) These nucleosides can also be prepared as 5'-O- phosphates. These nucleosides are useful as antiviral agents. (p. 5, lines 10-17)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the nucleosides of Lin et al. by adding a 5'-O- phosphate. One of ordinary skill in the art would have been motivated to do so because Gosselin et al. discloses that nucleoside phosphates having a similar structure are useful as antiviral agents. One of ordinary skill in the art would reasonably have expected success because phosphates are a common and routine prodrug moiety to attach to nucleosides.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 31-38, 46-50, 52, and 55-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin et al. (US patent 5627160, Reference of record in previous office action) in view of Gosselin et al. (PCT international publication WO00/26225, Reference included with PTO-892) Lin et al. discloses compounds and pharmaceutical compositions that are useful for treating viral infections including HBV. (column 3, line 17 – column 4, line 37) Embodiments of this invention include the nucleosides β-L-dideoxycytidine and β-L-5-fluoro-dideoxycytidine. (column 5, lines 33-52) Lin et al. does not disclose pharmaceutical compositions comprising the monophosphates or other pharmaceutically acceptable leaving groups of these nucleosides.

Gosselin et al. discloses β-L-2-azido fluorocytidine nucleosides having a structure similar to the dideoxy nucleosides of Locatelli et al. (p. 4, bottom of page) These nucleosides can also be prepared as 5'-O- phosphates. These nucleosides are useful as antiviral agents. (p. 5, lines 10-17)

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the nucleosides of Lin et al. by adding a 5'-O- phosphate. One of ordinary skill in the art would have been motivated to do so because Gosselin et al. discloses that nucleoside phosphates having a similar structure are useful as antiviral agents. One of ordinary skill in the art would reasonably have expected success because phosphates are a common and routine prodrug moiety to attach to nucleosides.

Thus the invention taken as a whole is *prima facie* obvious.

Conclusion

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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